

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
14 October 2004 (14.10.2004)

PCT

(10) International Publication Number  
**WO 2004/087660 A1**

(51) International Patent Classification<sup>7</sup>: **C07D 211/32**

(21) International Application Number:  
PCT/IN2003/000136

(22) International Filing Date: 2 April 2003 (02.04.2003)

(25) Filing Language: English

(26) Publication Language: English

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(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,

CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Declarations under Rule 4.17:**

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- of inventorship (Rule 4.17(iv)) for US only

**Published:**

- with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: A NOVEL PROCESS FOR AMORPHOUS FORM OF DONEPEZIL HYDROCHLORIDE

(57) Abstract: The present invention provides a novel process for the preparation of donepezil hydrochloride.

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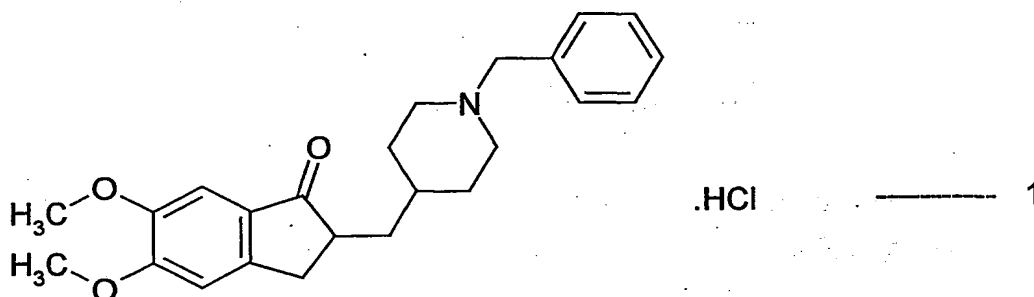
**A NOVEL PROCESS FOR AMORPHOUS FORM OF DONEPEZIL**  
**HYDROCHLORIDE**

**FIELD OF THE INVENTION**

5           The present invention provides a novel process for the preparation of donepezil hydrochloride.

**BACKGROUND OF THE INVENTION**

10          Donepezil hydrochloride of formula (1):



15       or 2,3-Dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1H-inden-1-one hydrochloride is useful for prevention and treatment of alzheimer disease. The therapeutic uses of donepezil hydrochloride and related compounds are disclosed in EP 296560. Amorphous form of donepezil hydrochloride is mentioned in US 6,140,321.

20          We have discovered a simple novel process for the preparation of amorphous form of donepezil hydrochloride.

          The object of the present invention is to provide a novel process for the preparation of the amorphous of donepezil hydrochloride.

**DETAILED DESCRIPTION OF THE INVENTION**

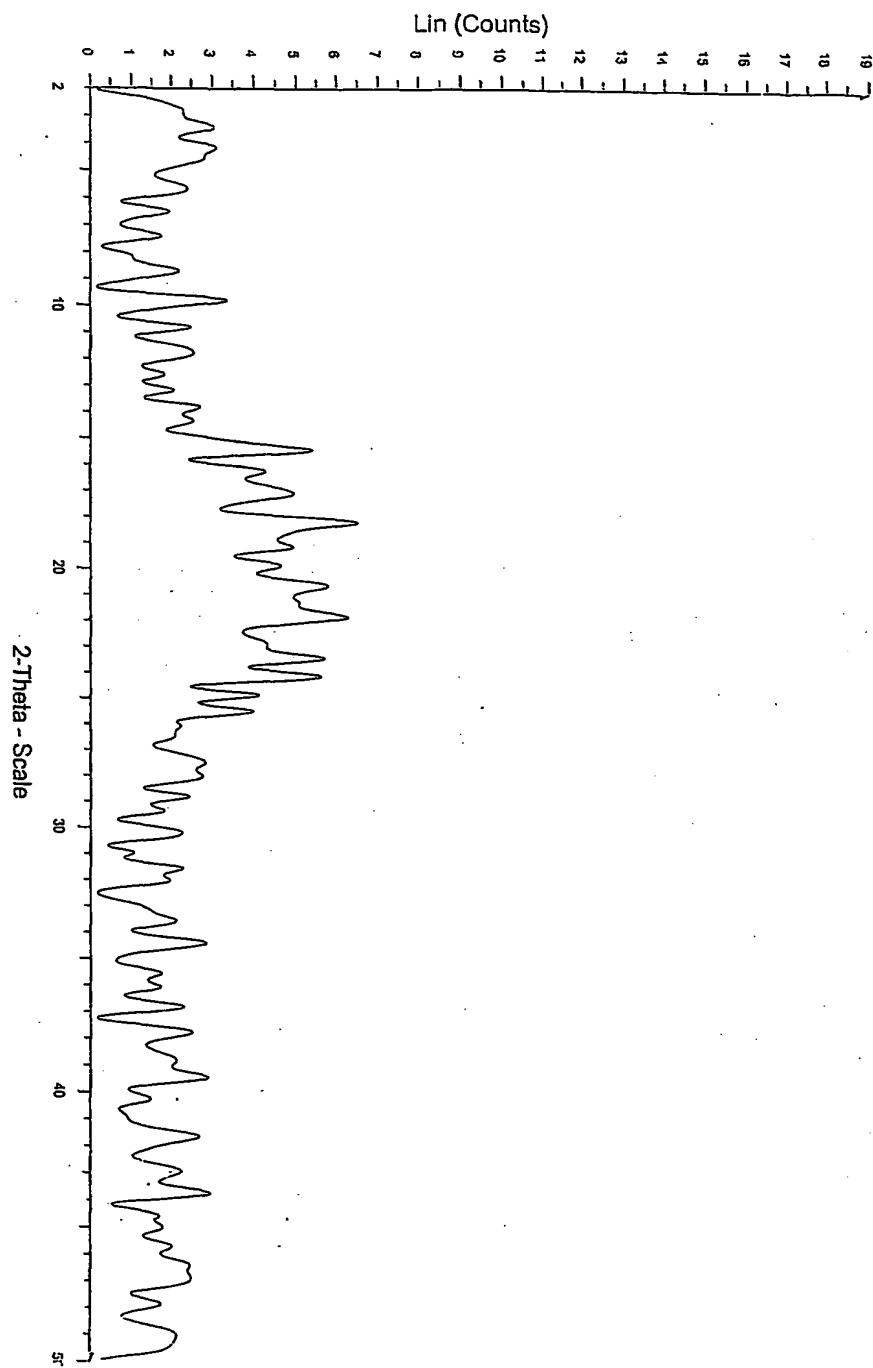
25          The amorphous donepezil hydrochloride is characterized by having broad x-ray diffraction spectrum as in figure 1.

Crystalline donepezil hydrochloride (10 gm) is dissolved in the mixture of ethanol (60 ml) and chloroform (50 ml). The solution is subjected to vacuum drying at about 45°C for 9 hours to give 9.2 gm of amorphous donepezil hydrochloride.

5

#### Example 4

Example 3 is repeated by subjecting the solution to spray drying using nitrogen gas instead of vacuum drying to give amorphous donepezil hydrochloride.



# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IN 03/00136-0

## CLASSIFICATION OF SUBJECT MATTER

IPC<sup>7</sup>: C07D 211/32

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC<sup>7</sup>: C07D 211/32

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPOQUE: WPI, PAJ, EPODOC, NPL, MEDLINE, XPESP databases; STN Karlsruhe CAS: REGISTRY and CA databases

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5985864 A (IMAI ET AL.) 16 November 1999 (16.11.99) <i>example 108.</i>	1-4
A	EP 1048653 A1 (ESAI CO., LTD.) 2 November 2000 (02.11.00) <i>examples.</i>	1-4

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

\* Special categories of cited documents:

„A“ document defining the general state of the art which is not considered to be of particular relevance

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„O“ document referring to an oral disclosure, use, exhibition or other means

„P“ document published prior to the international filing date but later than the priority date claimed

„T“ later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

„X“ document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

„Y“ document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

„&“ document member of the same patent family

Date of the actual completion of the international search

1 December 2003 (01.12.2003)

Date of mailing of the international search report

21 January 2004 (21.01.2004)

Name and mailing address of the ISA/AT

Austrian Patent Office

Dresdner Straße 87, A-1200 Vienna

Facsimile No. 1/53424/535

Authorized officer

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Telephone No. 1/53424/348

pat-in-198-04 25/10/04

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International application No.  
**PCT/IN 03/00136-0**

Patent document cited in search report			Publication date	Patent family member(s)			Publication date
EP	A	1048653	2000-11-02	US	B	6245911	2001-06-12
				WO	A	9929668	1999-06-17
US	A	5985864		CA	A	2252806	1997-12-11
				DE	T	69718216T	2003-10-09
				TW	B	513409	2002-12-11
				ES	T	2188946T	2003-07-01
				PT	T	1019374T	2003-03-31
				DK	T	1019374T	2003-04-07